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EXAMINER	
BARTON, JEFFREY THOMAS	
ART UNIT	**PAPER NUMBER**
1753	

DATE MAILED: 08/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	10/057,354	BOHM ET AL.
	Examiner	Art Unit
	Jeffrey T Barton	1753

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 October 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20020709, 20020723*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *PTO-1449, Paper No. 20021021*.

DETAILED ACTION

Specification

1. The disclosure is objected to because of the following informalities: lack of a definition. On Page 12, line 33, a formula for the number of holes (H) needed in a prior art microplate is given as 5N/4 + 7, without defining N. Please revise to include a definition of N as the number of samples to be analyzed.

Appropriate correction is required.

Claim Objections

2. Claim 15 is objected to because of the following informalities: an omitted word. The preamble reads "The separation of claim 12" instead of "The separation device of claim 12." Appropriate correction is required.

3. Claim 25 is objected to because it is an exact duplicate of claim 13. Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 16 recites the limitation "said reservoir array layer" in the second line of the claim. There is insufficient antecedent basis for this limitation in the

claim, as no reservoir array layer was previously discussed. The claim is treated herein as specifying that the electrode array is coupleable to the reservoirs of the device.

6. Claim 20 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The recited limitation of the number of holes being "approximately equal to the number of samples . . ." does not sufficiently define the metes and bounds of the claim, since it is not clear how large a difference between the number of samples and holes would result in the numbers no longer being "approximately equal."

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-5, 7, 8, 12-26, 30-36, and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simpson et al in view of either Howitz et al or Arnold et al.

Relevant to claim 1, Simpson et al disclose a separation device (Column 1, line 65 - Column 2, line 1) comprising: one or more anode reservoirs (Figure

1, 180; Column 9, lines 25-27)); a plurality of separation channels connected to the anode reservoirs (Column 3, lines 14-28; Column 9, lines 25-27), with each of the separation channels having an interior bounded by a side wall (Figure 4B; Column 4, line 47 - Column 5, line 7); a plurality of fluid inlets to the separation channels (Figure 2, B and C with associated channels to channel 222); and at least one cathode reservoir multiplexed with two or more separation channels. (Figure 1, Reservoir 120)

Relevant to claim 12, Simpson et al disclose a separation device comprising: an array of microfabricated separation channels formed at the surface of a first microfabricated substrate and a corresponding surface of a second substrate bonded to the surface of the first substrate with each channel having an interior bounded by a sidewall, a first end and a second end (Figures 1 and 4B; Column 9, lines 12-17; Column 4, line 47 - Column 5, line 7); an array of fluid inlets to the separation channels (Figures 1 and 2, B and C with associated channels to channel 222); an array of cathode reservoirs connected to the first end of each of the separation channels (Figure 1; Column 9, lines 23-24); and an array of anode reservoirs, wherein at least one anode reservoir is connected to the respective second ends of at least two of the separation channels. (Figure 1; Column 9, lines 25-27)

Relevant to claims 30 and 32, Simpson et al disclose a separation device comprising: a substrate (Column 4, line 47 - Column 5, line 7); a plurality of separation channels formed in the substrate (Column 3, lines 14-28), each channel having an interior bound by a side wall (Figure 4B; Column 4, line 47 -

Column 5, line 7); a plurality of fluid inlets to the separation channels (Figure 2, B and C with associated channels to channel 222); an anode reservoir multiplexed to two or more separation channels (Figure 1, Reservoir 180; Column 10, lines 49-57); and a cathode reservoir multiplexed to two or more separation channels (Figure 1, Reservoir 120; Column 10, lines 58-65)

Relevant to claims 2, 16, 17, 22, and 34, Simpson et al disclose an electrode array coupled or coupleable to the reservoirs and fluid inlets within the separation device. (Column 5, line 36 - Column 6, line 37; Column 10, lines 9-10) This array can be in electrical contact with the device (Figure 4B; Column 10, lines 31-33), or integral with the substrates of the device (Column 10, lines 11-13).

Relevant to claim 3, Simpson et al disclose a separation device with an outer perimeter and a center, with the separation channels connecting the outer perimeter to the center. (Figure 9; Column 9, lines 9-11)

Relevant to claims 8 and 26, Simpson et al disclose their device being a capillary array electrophoresis plate. (Column 1, lines 65-66)

Relevant to claim 14, Simpson et al disclose the first and second substrates being made of glass. (Column 9, lines 66-67)

Relevant to claim 15, Simpson et al disclose the first and second substrates being made of plastic. (Column 10, lines 1-2)

Relevant to claims 18 and 35, Simpson et al disclose the regular spacing of the fluid inlets on one of the substrates to receive solutions from a parallel loading device. (Column 1, lines 13-15; Column 4, line 47 - Column 5, line 7)

Relevant to claims 19 and 24, Simpson et al disclose the first substrate of their device including an array of electrodes aligned with sample reservoirs of the device to make electrical contact with solutions in the sample, waste, anode, and cathode reservoirs. (Column 10, lines 17-23)

Relevant to claim 20, Simpson et al disclose a number of holes, H, approximately equal to 5N/4, where N is the number of samples to be processed. (Column 10, lines 24-27)

Relevant to claim 21, Simpson et al disclose their device being made of a combination of glass and plastic. (Column 10, lines 28-30)

Relevant to claim 23, Simpson et al disclose a plurality of sample fluid inlets in communication with on of the separation channels (e.g. Figure 2, B and C both feed channel 222)

Relevant to claim 36, Simpson et al disclose a parallel loading device comprising a multi-headed pipetter. (Column 11, lines 16-18)

Relevant to claim 38, Simpson et al disclose the disposition of the separation channels in a radial pattern on the separation device. (Figure 9)

Simpson et al do not explicitly disclose a device comprising: fluid interface ports formed in the side walls of the separation channels to provide access to the interiors of the separation channels, wherein a separation medium disposed in the interior of the separation channel forms a virtual wall at each fluid interface port, and wherein each separation channel has at least one dedicated fluid interface port. They also do not explicitly disclose fluid interface ports with: dead

volumes less than about 1 nL (Claim 4), zero dead volume (Claim 5), or diameters between 25 and 125 μm (Claims 7, 13, 25, 31, and 33)

Howitz et al disclose a device (Figure) comprising: fluid interface ports (capillaries containing menisci 6) formed in the side wall of a fluid channel (9) to provide access to the interior of the fluid channel, wherein a separation medium disposed in the interior of the fluid channel forms a virtual wall at each fluid interface port (Menisci 6). They also disclose a fluid interface port with a diameter between 25 and 125 μm (Column 3, lines 12-15, length and width are 50 μm)

Arnold et al disclose a device comprising: a fluid interface port formed in the side walls of the separation channels to provide access to the interiors of the separation channels (Figure 6, port 630), wherein a separation medium disposed in the interior of the separation channel would form a virtual wall at each fluid interface port. They also disclose a fluid interface port with a diameter between 25 and 125 μm (Column 1, lines 33 and 34 give typical channel dimensions, diameter of 630 is illustrated in Figure 6 as being less than half the channel width)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Simpson et al by replacing the sample and waste reservoirs, and their associated side channels with a simple hole or holes through the sidewall to serve as a fluid port, as taught by either Howitz et al or Arnold et al, because it would simplify device construction and reduce sample waste.

Further addressing claims 4 and 5, given the definition of dead volume presented in the instant specification (roughly, the volume of liquid held in the port and not flowing with the fluid within the channel), the dead volume associated with ports such as those of Howitz et al will be a function of the affinities of the fluids for the surface of the port. As such, the dead volume will be zero or near zero for any clean hydrophobic port surface in a device using aqueous fluids. Such hydrophobicity is an innate property of many polymers (e.g. fluoropolymers) and can be achieved by using known surface treatments for glass (hexamethyldisilazane, used by Simpson - Column 4, lines 53-56) and silicon (Hydrofluoric acid), and would constitute an obvious modification of the device, because such a surface would minimize loss of the injected sample.

Further addressing claim 20, by replacing each sample reservoir with a fluid interface port, and eliminating waste reservoirs, the number of holes in this combination device would be reduced to N+A+C, where N is the number of samples to be analyzed, A is the number of anode reservoirs, and C is the number of cathode reservoirs. This sum approaches N as the degree of multiplexing of electrode reservoirs to plural channels increases, and thus is approximately equal to N with a geometry such as shown in Figure 8 of Simpson et al.

9. Claims 1 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simpson et al in view of either Howitz et al or Bass.

Simpson et al disclose a separation device (Column 1, line 65 - Column 2, line 1) comprising: one or more anode reservoirs (Figure 1, 180; Column 9, lines 25-27)); a plurality of separation channels connected to the anode reservoirs (Column 3, lines 14-28; Column 9, lines 25-27), with each of the separation channels having an interior bounded by a side wall (Figure 4B; Column 4, line 47 - Column 5, line 7); a plurality of fluid inlets to the separation channels (Figure 2, B and C with associated channels to channel 222); and at least one cathode reservoir multiplexed with two or more separation channels. (Figure 1, Reservoir 120)

Simpson et al do not explicitly disclose one or more fluid interface ports formed in the side walls of the separation channels to provide access to the interiors of the separation channels, wherein a separation medium disposed in the interior of the separation channel forms a virtual wall at the fluid interface port, nor do they disclose a fluid interface port that comprises and array of apertures forming virtual walls.

Howitz et al disclose a device (Figure) comprising a fluid interface port comprising an array of apertures forming virtual walls (Figure, capillaries containing menisci 6), wherein the virtual walls are formed from the fluid within a flow channel (9), and the interface port provides access to the interior of the flow channel.

Bass discloses a device for liquid transfer (Figure 1b) comprising a fluid interface port comprising an array of apertures (12) forming virtual walls (upon fluid contact with apertures), and the interface port provides access to a fluid

receptacle (17). Bass also suggests the utility of this device for fluid transfer in microfluidic applications. (Column 2, lines 34-38)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Simpson et al by replacing the sample and waste reservoirs, and their associated side channels with an array of holes through the sidewall to serve as a fluid port, as taught by either Howitz et al or Bass, because it would reduce the number of electrodes needed for device operation.

10. Claims 9-11 and 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simpson et al and either Howitz et al or Arnold et al as applied to claims 1 and 12 above, and further in view of Bjornson et al.

Simpson et al and Howitz et al disclose combinations as described above in addressing claims 1 and 12. Simpson et al and Arnold et al also disclose combinations as described above in addressing claims 1 and 12.

None among Simpson et al, Howitz et al, and Arnold et al disclose their devices being used for electrochromatography (Claims 9 and 27), pressure-driven chromatography (Claims 10 and 28), or isoelectric focusing (Claims 11 and 29).

Bjornson et al disclose electrophoretic devices used for isoelectric focusing and capillary chromatography. (Column 12, lines 53-59) They also disclose fluid flow in their devices by electroosmosis (Column 11, lines 55-60),

which suggests electrochromatography. (i.e. chromatography in which the motion of the mobile phase is caused by an electric field)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combination of either Simpson et al and Howitz et al or Simpson et al and Arnold et al by providing the separation capillaries with a chromatographic medium, immobilized pH gradient, or ampholytes and using the device for electrochromatography or isoelectric focusing, as taught by Bjornson et al, because it would provide useful analytical data about the analytes.

Additionally, electroosmotic force corresponds to a type of pressure driving a fluid through a capillary, and as such, is considered a form of pressure-driven chromatography.

11. Claim 37 is rejected under 35 U.S.C. 103(a) as being unpatentable over Simpson et al and either Howitz et al or Arnold et al as applied to claim 36 above, and further in view of Sundberg et al.

Simpson et al and Howitz et al disclose a combination as described above in addressing claim 36. Simpson et al and Arnold et al also disclose a combination as described above in addressing claim 36.

None among Simpson et al, Howitz et al, and Arnold et al disclose a parallel loading device comprising a pin for carrying and introducing the droplet of a liquid sample to the fluid interface port by contacting the virtual wall.

Sundberg et al disclose a parallel loading device (Figure 2) comprising a pin (38) for carrying and introducing the droplet of a liquid sample (36) to the ports (34) of a microfluidic system.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combination of either Simpson et al and Howitz et al or Simpson et al and Arnold et al by providing a parallel loading device comprising pins for carrying liquid samples to the fluid interface port, as taught by Sundberg et al, because it would simplify delivery of small droplets.

12. Claim 39 is rejected under 35 U.S.C. 103(a) as being unpatentable over Simpson et al in view of Howitz et al.

Simpson et al and Howitz et al disclose a combination device that was described above in addressing claims 1, 12, 30, and 32.

Simpson et al disclose a method of injecting a liquid into a separation device, comprising: connecting a cathode reservoir to the respective first ends of two or more channels (Column 11, lines 29-30), connecting an anode reservoir to the respective second ends of these channels (Column 11, lines 31-32), and loading a sample liquid into the sample reservoir and applying a voltage to inject the sample into the separation channel. (Column 8, lines 32-41; Column 11, lines 33-41)

Simpson et al do not explicitly disclose forming a droplet from the liquid sample, or directing the droplet to a virtual wall formed by a separation medium in a fluid interface port formed in the side wall of a separation channel.

Howitz et al disclose forming a droplet from the liquid sample (Figure, droplet 5; Column 3, lines 31-34), and directing the droplet to a virtual wall formed by a liquid in a fluid interface port formed in the side wall of a flow channel.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Simpson et al by altering the injection step by: forming a droplet of the sample and directing it to the virtual wall formed at a fluid interface port by a liquid in the separation channel (in the combination device of Simpson et al and Howitz et al described above), as taught by Howitz et al, because it would reduce waste of the sample liquid.

13. Claims 40-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simpson et al in view of Howitz et al.

Relevant to claims 40 and 43, Simpson et al disclose a method of forming a separation device comprising the steps of: forming a plurality of separation channels in the device (Column 11, line 49), each channel being defined by an interior bounded by a side wall (Figure 4B; Column 4, line 47 - Column 5, line 7); forming a plurality of sample reservoirs connected to the channels (Column 11, lines 50-54); connecting an anode reservoir to two or more channels (Column 11, lines 55-56); and connecting a cathode reservoir to two or more channels. (Column 11, lines 66-67)

Relevant to claims 42 and 45, Simpson et al disclose the radial disposition of the channels on the separation device. (Figure 9)

Simpson et al do not explicitly disclose a method comprising: forming a plurality of fluid interface ports in the side walls of the separation channels to provide access to the interiors of the separation channels, wherein a separation medium disposed in the interior of the separation channel forms a virtual wall at each fluid interface port. They also do not explicitly disclose removing portions of the side walls to define fluid interface ports with diameters between 25 and 125 μm (Claims 41 and 44)

Howitz et al disclose formation of fluid interface ports (capillaries containing menisci 6) formed in the side wall of a fluid channel (9) to provide access to the interior of the fluid channel, wherein a separation medium disposed in the interior of the fluid channel forms a virtual wall at each fluid interface port (Menisci 6). (Column 3, lines 1-15) They also disclose forming a fluid interface port with a diameter between 25 and 125 μm (Column 3, lines 10-15, length and width are 50 μm)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Simpson et al by replacing the step of forming sample reservoirs and associated side channels with the formation of a simple hole or holes (50 μm length and width) through the sidewall to serve as a fluid port, as taught by Howitz et al, because it would simplify device construction and reduce sample waste.

Conclusion

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Jeffrey Barton, whose telephone number is (571) 272-1307. The examiner can normally be reached Monday-Friday from 8:30 am – 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen, can be reached at (571) 272-1342. The fax number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

JTB
August 5, 2004

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